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The psychosocial correlates of transplant survival

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Abstract

Background: due to the shortage of organs, half of the patients on the waiting list for transplantations die. Clinicians have a duty to identify those patients whom might benefit most. The correlation between psychosocial factors and survival in children who have received lung transplantation for CF has not been investigated. *Aims:* to examine: (1) differences in physical, demographic and psychological factors between two groups of children with CF, those who did or did not survive the waiting period for transplantation. (2) Correlations between these factors pre-transplantation and length of survival post transplantation. *Methods:* 81 children—mean age 11 years 6 months—and their parents underwent semi-structured standardised interviews and completed standardised instruments prior to being placed on the transplantation waiting list. The following domains were measured: child's disability, psychiatric status and self-esteem; quality of marital relationship and parental psychiatric status; and family attitudes and functioning. *Results:* 20% of the children on the waiting list had a psychiatric disorder and 60% of the parents scored within the psychiatric disorder range. One third of the parents had marital difficulties, and 20% of the families showed chaotic functioning. Only half of the children survived to receive transplantation. Survivors and non-survivors were comparable with regard to all psychological measures. A follow up of the transplanted children, ranging from 3 to 156 months post-transplantation, produced a group of nine survivors and 30 non-survivors. Only two pre-transplant factors showed a significant association with length of survival after transplantation. Severe physical disability was associated with longer survival ($P=0.01$), and parental hostility to partner was associated with a shortened life span ($P=0.04$). No other factors were significantly associated with length of survival. *Conclusion:* there is no evidence to suggest that adverse psychosocial factors should be used as a contraindication to transplantation.

Keywords: Cystic fibrosis; Resilience; Family; Paediatrics; Transplantation; Expressed emotion

1. Introduction

While the number of patients on transplant waiting lists has increased, the number of transplants performed has remained constant due to a limited supply of suitable donor organs (Unos data source, 2002). In our centre, over half of CF patients listed for transplant die whilst on the waiting list [1]. Because of the significant shortage of organs, clinicians have a responsibility to maximise the benefit of the organs available, by identifying those patients whom might benefit most. A previous study in our centre found no evidence that 'clinical status' prior to transplant has any effect upon the post-transplant survival of children with cystic fibrosis [2]. A key question is whether adverse psychological factors prior to transplantation affect outcome survival. Transplant teams often use these as a contraindication, suggesting that such families would not be able to cope with the stresses associated with transplantation and that survival would, therefore, be compromised.

Studies conducted in community settings have shown that even among children exposed to the most serious disadvantages it is unusual for more than half of those to be adversely affected, and that there are large individual variations in response to adverse events and circumstances [3,4]. Resilience involves several related elements: (a) a sense of self-esteem/confidence; (b) belief in one's one self-efficacy and ability to deal with change and adaptation; and (c) a repertoire of problem-solving approaches [4].

Psychosocial research on life-threatening conditions has in recent years focused on identifying those protective factors that foster resilience and mediate illness outcome, including survival. Most studies on transplant

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recipients have been conducted with adults, and the results are inconclusive [5–7]. Only two studies have investigated the influence of psychosocial factors on transplant survival in the paediatric population [8,9]. The first failed to find any positive correlations between positive parent–child interaction, parental emotional support, enthusiasm for the procedure, child's motivation and post bone marrow transplant survival [8]. In the second study, two groups of children were compared, those who did or did not survive 12-months post bone marrow transplantation [9]. Non-survivors scored higher in both illness severity and complications than survivors. The child's functional impairment, family dysfunction and whether the child was perceived as being more likeable and co-operative accounted for 36% of the variance.

Studies investigating the protective and risk factors associated with post-transplant survival in the CF population are lacking. The aims of this study were to examine:

1. Differences in physical, demographic and psychological factors between two groups of children with CF, those who did or did not survive the waiting period for transplantation.
2. Correlations between these factors pre transplantation and length of survival post transplantation.

2. Methods

Participants were children who were consecutively referred for transplantation to Great Ormond Street Hospital NHS Trust between December 1988 and June 1995, and their parents. Four weeks prior to the assessment of suitability for transplantation, the families were mailed a package containing: (a) general information about the routine assessment process and (b) information about the research and consent forms.

Following admission, the families were approached by the author and informed consent was obtained following the Research Ethics Committee procedures. Inclusion criteria were that: (i) the child was placed on the waiting list; (ii) written informed consent was obtained; (iii) English language was good enough to complete psychological assessment; (iv) the child appeared to be within a normal range of intelligence; and (v) had no other chronic condition.

2.1. Assessment

All children underwent a detailed physical examination. Physical disability was measured on an Index of Physical Ability, rated by the physicians from 'no disability' to 'severe disability,' (e.g. uses buggy/wheelchair and oxygen treatment) [10]. Psychological assessment consisted of a semi-structured standardised psychiatric interview [11]. The interview was audio-recorded, and the presence or absence of psychiatric illness was rated independently by the authors using the ICD-10 classification of mental and behavioural disorders [12]. Children, aged 8 and older, also completed the Piers–Harris Children's Self-Concept Scale [13].

Parental attitudes towards both the ill child and partner were assessed with the expressed emotion scales, which are derived from the Camberwell Family Interview (CFI) [14]. The CFI measures five attitudes: overinvolvement; warmth; hostility; frequency of critical comments; and frequency of positive remarks. This instrument was chosen because it measures the family emotional climate, and previous research has shown that the overinvolvement, critical comments and hostility subscales have a predictive value with regard to outcome in mental and physical disorders. All interviews were audio-recorded, transcribed and rated independently by two trained raters. Intra-class correlation among raters ranged from 0.76 to 0.97.

Family functioning was rated independently by the clinical nurse specialist and the first author on a three-point scale: good; moderate; and chaotic functioning [15]. The intra-class correlation was 0.91, and disagreements about the ratings were resolved through discussion.

Demographic data about the family were obtained from the parental interviews. Parents completed the Golombock Rust Inventory of Marital State (GRIMS) [16] to assess the quality of the marital relationship and the General Health Questionnaire (GHQ-28) [17], to detect psychiatric disorder.

2.2. Statistical analyses

The statistical package for the social sciences (SPSS, 1999) was used to analyse the data. Selected parametric and non-parametric tests were used for comparisons between children who survived the waiting period for transplantation and those who did not. Relationships between the demographic, illness-related and psychosocial variables measured pre-transplantation and survival time after transplantation were studied using Cox proportional hazard models. Length of survival was calculated in months from time of transplantation to time of death or, for those still living, to time of data analysis. The status variable was the outcome at the time data analysis (alive death). A level of 0.05 was used as a criterion for statistical significance. Because of the number of potential predictor variables examined relative to our sample size, variables were entered in the initial model in stages, similar to the approach used by Andrykowski et al. [18].

3. Results

Of the 84 families who met inclusion criteria, two refused participation and one child was removed from

Table 1
Child's illness-related and demographic characteristics

	Mean (S.D)
Age: range 4.6–17.1 (years, months)	11.5 (2.9)
FVC: range 14–90	44.8 (16.4)
FEV1: range 13–71	33.7 (12.1)
% Weight for height: range 54–120	84.8 (13.12)
	N (%)
Males	46 (57.0)
Females	35 (43.0)
Families who had lost a child previously	14 (17.3)
Families with more than one child with CF	17 (21.0)
Ability index (physicians' report; n=80)	
Some disability	19 (23.7)
Moderate disability	16 (20.0)
Severe disability	45 (56.3)
Family structure: (*n=81*)	
Living with both natural parents	57 (70.4)
Living with a single parent	11 (13.6)
Living with reconstituted/adoptive family	13. (16.0)

the waiting list, as he experienced a significant improvement in physical health. The families of 81 children participated, and their characteristics are presented in Table 1 and Table 2. (There was variation regarding completion of instruments. Only 50 children completed the Piers and Harris Self-Concept Scale, because of the child's young age or severity of illness. Parents in 61 families completed the GHQ-28 scale. Eleven parents did not complete the marital scale as they were single.) Twenty percent of the children and 60% of the parents scored within the psychiatric disorder range; and 20% of the families scored within the range of chaotic functioning.

3.1. Group differences at baseline

Less than half of the children survived to receive transplantation. Comparison of survivors and non-survivors are presented in Table 3 and Table 4. There were no statistical differences between the groups with the exception that a higher proportion of parents in the non-survivor group scored within the psychiatric range, suggesting a higher level of distress.

3.2. Relation to survival

Nine out of 39 children who received transplantation were still alive at the completion of the study. Table 5 illustrates the univariate Cox survival analyses of demographic, illness-related and psychological variables. Younger age and severe disability were associated with longer post-transplant survival. Pre-transplant hostility towards a marital partner was associated with shorter survival post transplantation. When these three variables were entered into a stepwise Cox regression model, the physical ability index and hostility, but not child's age, remained significantly associated with length of survival (model $\chi^2 = 17.29$; $P < 0.001$).

4. Discussion

This is the first study comparing characteristics of child survivors and non-survivors of the waiting period for transplantation; and examining length of post-transplant survival in relation to pre-transplant psychosocial measures. The results show that:

a. 20% of the children and 60% of the parents scored within the psychiatric disorder range at the time of assessment; and that 20% of the families scored within the range of chaotic functioning;
b. Child and family characteristics were similar in survivors and non-survivors of the waiting period for transplantation, although there was a higher level of distress at assessment in the parents of subsequent non-survivor;
c. Greater disability prior to transplantation was associated with increased survival post transplantation; whilst pre-transplantation parental hostility towards the partner was associated with shorter survival.

The levels of psychiatric and family morbidity found in the present study are higher than that reported in other studies [8,9]. The discrepancies might be due to differences in both the illnesses being studied and the research designs. There is a paucity of data with regard to differences between survivors and non-survivors while awaiting paediatric transplantation. The higher

Table 2
Child's and parents' psychological characteristics

Child's psychiatric illness (ICD-10; *n=81*)	16 (19.7)
Poor self-concept (Piers and Harris; *n=50*)	4 (8.0)
Parental psychiatric illness (GHQ-28; *n=61*)[a]	36 (59.0)
Poor marital relationship (GRIMS; *n=70*)[b]	8 (11.4)
Family functioning (*Schneiderman; n=81*)	
Good or moderate	64 (79.0)
Chaotic	17 (21.0)
Parental attitudes towards the Child (*CFI; n=79*)[c]	
Overinvolvement: low (ratings 0–3)	42 (53.2)
Warmth: high (ratings 4–5)	68 (86.1)
Critical comments: nil	48 (60.8)
Hostility: nil	73 (92.4)
Positive remarks: one or more	70 (88 6)
Parental attitudes towards partner (*CFI; n=71*)[d]	
Warmth: high (ratings 4–5)	40 (56.3)
Critical comments: nil	58 (81.6)
Hostility: nil	68 (95.7)
Positive remarks: one or more	29 (40.8)

[a] One or two parents scored above the cut off score on this scale.
[b] One or two parents scored above the cut off score on this scale.
[c] One or two parents scored within the specified range.
[d] One or two parents scored within the specified range.

Table 3
Comparison of demographic and illness-related characteristics

	Survivors		Non-survivors		Analysis
	$N=39$		$N=42$		
	N	%	*N*	%	
Female	18	46.2	28	66.7	
Male	21	53.8	14	33.3	$\chi^2=3.4$; d.f.=1; $P=0.07$
Loss of one sibling or more[a]	8/38	21.1	6/42	14.3	$\chi^2=0.63$; d.f.=1; $P=0.30$
Two or more children with CF[b]	9/38	23.7	8/42	19.0	$\chi^2=0.25$; d.f.=1; $P=0.40$
Parental separation[c]	12/39	30.8	10/42	23.8	$\chi^2=0.49$; d.f.=1; $P=0.32$
	Mean	S.D.	Mean	S.D.	
Age	11.4	3.04	11.7	2.8	$t=-0.5$; d.f.=79; $P=0.29$
FVC	43.1	15.0	48.2	20.0	$t=-1.2$; d.f.=79; $P=0.09$
FEV1	31.5	10.5	35.6	17.5	$t=-1.1$; d.f.=79; $P=0.36$
% Weight for height	82.7	14.7	86.7	11.1	$t=-1.3$; d.f.=79; $P=0.10$
Ability index (physicians' report)	3.5	0.7	3.1	0.8	$t=2.2$; d.f.=79; $P=0.13$
Survival rate at completion of study					
N	9		30		
Survival mean (S.D.) since *Tx* (months)	87.8 (38.2)		35.7 (28.0)		$F=1.2$; d.f.=37; $P=0.0001$
Range (months)	40–156		1–97		

[a] Coded as factor: absent [0] or present [1].
[b] Coded as factor absent [0] or present [1].
[c] Coded as factor absent [0] (living with natural parents) or present [1] (single or reconstituted family).

level of parental distress, as shown by the GHQ-28 ratings, found in the non-survivors when compared to the survivors is of interest in the context of previous reports: increased parental distress has been reported in association with greater severity of illness [19]. However, in the present study, the illness-related measures indicated no significant differences between the waiting list survivors and non-survivors, although there was a trend towards more disability in the latter group. It is possible that following the assessment, there were differences amongst the two groups with regard to medical course and other factors, (e.g. parental perception of illness severity, illness-related fears and negative responses from family and friends, hope) which were not measured in the study but have found to be mediators of parental distress in the literature on paediatric chronic illness [19–21].

In contrast with the findings of McConville et al. [9], this study failed to show that chaotic family functioning and psychiatric illness were risk factors associated with

Table 4
Comparison of psychological and family characteristics

	Survivors		Non-survivors		Analysis
	N	%	*N*	%	
Child's psychiatric illness	9/39	23.1	7/42	16.7	$\chi^2=0.5$; d.f.=1; $P=0.32$
Poor self-concept	2/22	9.1	2/28	7.1	$\chi^2=0.06$; d.f.=1; $P=0.59$
Parental psychological distress	13/29	44.8	23/32	71.9	$\chi^2=4.6$; d.f.=1; $P=0.04$
Marital disharmony	13/39	33.3	6/42	14.3	$\chi^2=4.0$; d.f.=1; $P=0.06$
Chaotic family functioning	12/39	30.8	5/42	11.9	$\chi^2=4.3$; d.f.=1; $P=0.05$
Parental attitude towards the child: CFI					
Overinvolvement: high	17/37	45.9	20/42	47.6	$\chi^2=0.22$; d.f.=1; $P=0.53$
Warmth: nil-moderate	7/37	18.9	4/42	9.5	$\chi^2=1.44$; d.f.=1; $P=0.33$
Critical comments: 1 or more	13/37	35.1	18/42	42.9	$\chi^2=0.49$; d.f.=1; $P=0.50$
Hostility; present	3/37	8.1	3/42	7.1	$\chi^2=0.02$; d.f.=1; $P=0.60$
Positive remarks: absent	5/37	13.5	4/42	9.5	$\chi^2=0.31$; d.f.=1; $P=0.41$
Parents attitude towards partner: CFI					
Warmth: nil-moderate	17/33	51.1	14/38	36.8	$\chi^2=1.54$; d.f.=1; $P=0.23$
Critical comments: 1 or more	6/33	18.2	7/38	18.4	$\chi^2=0.01$; d.f.=1; $P=1.0$
Hostility: present	2/34	5.9	1/38	2.6	$\chi^2=0.47$; d.f.=1; $P=0.45$.
Positive remarks: absent	22/33	66.7	20/38	52.6	$\chi^2=1.44$; d.f.=1; $P=0.16$

Table 5
Univariate cox survival hazard analysis

Variable	$B\psi$	S.E.	Wald statistics	P
Gender	−0.458	0.76	0.359	0.54
Age	0.382	0.20	3.59	0.05
Loss of one sibling or more	−0.821	1.09	0.557	0.45
Two or more children with CF	0.402	1.16	0.120	0.72
Unemployment	1.151	1.41	0.658	0.41
Parental separation	−1.358	1.11	1.475	0.22
FVC	0.028	0.03	0.851	0.35
FEV1	0.018	0.03	0.313	0.57
% Weight for height	−0.005	0.02	0.051	0.82
Ability index (physicians' report)	−1.09	0.49	4.950	0.02
Child's psychiatric illness	−0.360	0.82	0.189	0.66
Self-concept	0.214	0.13	2.480	0.11
Parental psychological distress	−0.735	0.84	0.765	0.38
Marital disharmony	0.857	0.73	1.380	0.24
Family functioning	−0.635	0.64	0.960	0.32
Parental attitude towards the child:				
Overinvolvement (EOI)	−1.580	1.09	2.070	0.15
Warmth (W)	−3.258	5.49	0.352	0.55
Critical comments (CC)	0.781	0.83	0.886	0.34
Hostility (H)	−3.077	14.53	0.045	0.83
Positive remarks (PR)	0.292	1.12	0.067	0.79
Parental attitude towards the partner:				
Warmth (W)	0.219	0.72	0.091	0.76
Critical comments (CC)	−0.507	0.87	0.338	0.56
Hostility (H)	2.889	1.41	4.169	0.04
Positive remarks (PR)	1.055	1.08	0.943	0.33

ψ A positive B weight indicates an association between higher scores on a variable and decreased length of survival.

a shorter length of survival post transplantation. Greater disability prior to transplantation was associated with an increased survival post transplantation. To understand this finding, correlations were conducted between all psychological and illness-related measures. A positive correlation was found between parental overinvolvement and disability ($r=0.385$; $P=0.01$). It is possible that parental overinvolvement has a beneficial effect on management of physiotherapy and other aspects of treatment, resulting in a better long-term outcome after transplantation. This study also showed that hostility towards the partner was associated with shorter survival. Everson et al. [22] found similar results with adults with heart disease. More research is needed exploring the predictive value of the expressed emotion scales.

5. Conclusions

There was a high rate of psychiatric disorder in the children and their parents, as well a high level of marital problems and family dysfunction. Psychosocial assessment should form part of the overall assessment and psychological treatments offered as required. The lack of strong associations between adverse psychosocial factors and length of survival suggests that the presence of adverse psychosocial factors should not be used as a contraindication to transplantation. Further research should be focused on identifying other factors that might be associated with resilience as a means of prolonging survival after transplantation.

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References

[1] Aurora P, Whitehead B, Wade A, Bowyer J, Whitmore P, Rees PG, et al. Lung transplantation and life extension in children with cystic fibrosis. Lancet 1999;354:591–3.
[2] Aurora P, Gassas A, Ehtisham S, Whitehead B, Whitmore P, Rees PG, et al. The effect of prelung transplant clinical status on post-transplant survival of children with cystic fibrosis. Eur Respir J 2000;16:1061–4.
[3] Wolff S. The concept of resilience. Aust N Z J Psych 1995;29:565–74.
[4] Rutter M. Resilience in the face of adversity: protective factors and resistance to psychiatric disorder. Br J Psych 1985;17:598–611.

[5] Broers S, Hengeveld M, Kaptein AA, Le Cessie S, van de Loo F, de Vries T, et al. Are pretransplant psychological variables related to survival after bone marrow transplantation? A prospective study of 123 consecutive patients. J Psychosom Res 1998;45:341–51.

[6] Molassiotis A, Van DA, Milligan DW, Goldman JM. Symptom distress, coping style and biological variables as predictors of survival after bone marrow transplantation. J Psychosom Res 1997;42:275–85.

[7] Chacko RJ, Harper RG, Gotto J, Young J. Psychiatric interview and psychometric predictors of cardiac transplant survival. Am J Psych 1996;153:1607–12.

[8] Pfefferbaum B, Lindamood MM, Wiley FM. Pediatric bone marrow transplantation: psychosocial aspects. Am J Psych 1977;134:1299–301.

[9] McConville BJ, Steichen-Asch P, Harris R, Neudorf S, Sambrano J, Lampkin B, et al. Pediatric bone marrow transplants: psychological aspects. Can J Psych 1990;35:769–75.

[10] Serrano-Ikkos E, Whitehead B, Lask B. Psychosocial morbidity in children, and their families, awaiting heart or heart-lung transplantation. J Psychosom Res 1997;42:253–60.

[11] Rutter M, Graham P. The reliability and validity of the psychiatric assessment of the child: interview with the child. Br J Psych 1968;114:563–79.

[12] WHO. TCD-10. Classification of mental and behavioural disorders World Health Organisation 1999. Geneva.

[13] Piers V.E., Harris D.B. Piers and Harris children's self-concept scale Western Psychological Services 1984. Los Angeles, California.

[14] Vaughn CE, Left J. The measurement of expressed emotion in the families of psychiatric patients. Br J Soc Clin Psych 1976;15:165.

[15] Schneiderman G, Lowden JA, Rae-Grant Q. Family reactions, physician responses and management issues in fatal lipid storage diseases. Clin Paediatr 1976;15:887–90.

[16] Rust J., Bennun I., Crowe M., Golombok S. The Golombok Rust Inventory of Marital State (GRIMS). NFER-NELSON, 1985.

[17] Goldberg I. General health questionnaire (GHQ-28). NFER-NELSON, 1978.

[18] Andrykowski MA, Brady MJ, Henslee-Downey PJ. Psychosocial factors predictive of survival after allogenic bone marrow transplantation for leukemia. Psychosom Med 1994;56:432–9.

[19] Horton TV, Wallander JL. Hope and social support as resilience factors against psychological distress of mothers who care for children with chronic physical conditions. Rehabil Psychol 2001;46:382–99.

[20] Kazak AE, Stuber ML, Barakat ML, Meeske K, Guthrie D, Meadows AT, et al. Predicting posttraumatic stress symptoms in mothers and fathers of survivors of childhood cancers. J Am Child Acad Child Adoles Psych 1998;38:823–31.

[21] Manne S, DuHamel K, Nereo N, Ostroff J, Parson S, Martini R, et al. Predictors of PTSD in mothers of children undergoing bone marrow transplantation: the role of cognitive and social processes. J Pediatr Psychol 2002;27:607–19.

[22] Everson SA, Kauhanen J, Kaplan GA, Goldberg DE, Julkunen J, Tuomilento J, Salonen JT, et al. Hostility and increased risk of mortality and acute myocardial infarction: the mediating role of behavioural risk factors. Am J Epidemiol 1997;15:142–52.